UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/565,239	01/19/2006	Hiroshi Kase	00005.001285.	9168

5514 7590 10/20/2009

FITZPATRICK CELLA HARPER & SCINTO
1290 Avenue of the Americas
NEW YORK, NY 10104-3800

EXAMINER	
PIHONAK, SARAH	
ART UNIT	PAPER NUMBER
1627	
MAIL DATE	DELIVERY MODE
10/20/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/565,239	KASE ET AL.	
	Examiner	Art Unit	
	SARAH PIHONAK	1627	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 June 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,8,9,20,26,27,41,51 and 52* is/are pending in the application.

4a) Of the above claim(s) *20,26,27,41,51 and 52* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,8 and 9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This application is a 371 (national stage application) of PCT/JP04/10758, filed on 7/22/2004.

Priority

This application, filed on 1/19/2006, also claims foreign priority to Application No. 2003-201549, filed on 7/25/2003.

Response to Arguments

1. In the office action dated 2/2/2009, claim 38 was rejected under 35 USC § 102(b) as being anticipated by Shimada et. al., WO 99/12546 (for convenience, reference is made to US Patent No. 6,727,259). In the response filed on 6/30/2009, claim 38 was cancelled; therefore this rejection is moot. Claims 1, 3, 8, and 9 had also been previously rejected under 35 USC § 103(a) as being unpatentable over Greenlee et. al., WO 03/022283 Patent Publication, in view of Shimada et. al. (WO 99/12546, or US Patent No. 6,727,259). Claim 3 has been cancelled, and the rejection of this claim is considered moot. In response to the rejection of remaining claims 1, 8, and 9, the Applicants have submitted a declaration under 37 C.F.R. § 1.132. The Applicants have stated that the declaration shows results in which the combination of the selective serotonin reuptake inhibitors paroxetine hydrochloride or fluoxetine hydrochloride and (E)-8-(3,4-dimethoxystyryl)-1,3-diethyl-7-methyl-3,7-dihydro-1H-purine-2,6-dione is considerably more effective for treating depression in comparison to either agent administered alone. Therefore, the Applicant has argued that as the combination

of a selective serotonin reuptake inhibitor and (E)-8-(3,4-dimethoxystyryl)-1,3-diethyl-7-methyl-3,7-dihydro-1H-purine-2,6-dione is not taught by the prior art, the claims are not obvious. The Applicants' arguments, as well as the declaration, have been fully considered, but are not found to be persuasive. While it is noted that the results show that the combination of (E)-8-(3,4-dimethoxystyryl)-1,3-diethyl-7-methyl-3,7-dihydro-1H-purine-2,6-dione and fluoxetine hydrochloride demonstrate synergy, this combination is at a specific dosage of each compound. Particularly, the declaration shows synergistic results in which fluoxetine hydrochloride is at a dosage of 10 mg/kg, and (E)-8-(3,4-dimethoxystyryl)-1,3-diethyl-7-methyl-3,7-dihydro-1H-purine-2,6-dione is administered at a dosage of 0.04 mg/kg. However, the claims are not limited to a combination of (E)-8-(3,4-dimethoxystyryl)-1,3-diethyl-7-methyl-3,7-dihydro-1H-purine-2,6-dione and fluoxetine hydrochloride in these specific dosages. The claims are directed to a combination of (E)-8-(3,4-dimethoxystyryl)-1,3-diethyl-7-methyl-3,7-dihydro-1H-purine-2,6-dione and a selective serotonin reuptake inhibitor, in any dosage. Therefore, the results presented by the declaration are not commensurate in scope with the claims. Greenlee et. al. teaches that the combination of an adenosine A2A antagonist and a selective serotonin reuptake inhibitor is beneficial for treating depression, while Shimada et. al. teaches that (E)-8-(3,4-dimethoxystyryl)-1,3-diethyl-7-methyl-3,7-dihydro-1H-purine-2,6-dione is an adenosine A2A antagonist effective in treating a variety of conditions, including neurodegenerative disorders and depression. Therefore, it would have been prima facie obvious to one of ordinary skill in the art to combine (E)-8-(3,4-

dimethoxystyryl)-1,3-diethyl-7-methyl-3,7-dihydro-1H-purine-2,6-dione with a selective serotonin reuptake inhibitor such as fluoxetine or its well known hydrochloride salt, because the prior art teaches that the combination of an adenosine A2A receptor antagonist and a selective serotonin reuptake inhibitor such as fluoxetine are beneficial in treating depression. For Applicants' convenience, this rejection will be restated for claims 1, 8, and 9 below. Accordingly, this action is made **FINAL**.

Claims 2-7, 10-19, 21-25, 28-40, and 42-50 have been cancelled by the Applicants. In the reply filed on 6/30/2009, new claims 51 and 52 were added. However, as claims 51 and 52 are drawn to a method of treating depression, and are not included in the elected invention of Group I, which is a composition, these claims are withdrawn from current examination. Claims 20, 26, 27, and 41 had been previously withdrawn due to the restriction requirement. Claims 1, 8, and 9, which are drawn to the Applicants' elected invention of Group I, were examined, with regards to the species elected by the Applicants, (E)-8-(3,4-dimethoxystyryl)-1,3-diethyl-7-methyl-3,7-dihydro-1H-purine-2,6-dione, and fluoxetine hydrochloride (as the selective serotonin reuptake inhibitor).

2. Claims 1, 8, and 9 were examined.

3. Claims 1, 8, and 9 are rejected.

Claim Rejections-35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1, 8 & 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Greenlee et. al., WO 03/022283 Patent Publication, in view of Shimada et. al., WO 99/12546, in which the English version US Patent No. 6,727,259 is referenced for convenience.

The claims are drawn to a pharmaceutical composition comprised of (E)-8-(3,4-dimethoxystyryl)-1,3-diethyl-7-methyl-3,7-dihydro-1H-purine-2,6-dione and the selective serotonin reuptake inhibitor, fluoxetine hydrochloride.

Greenlee et. al. teaches that the combination of an adenosine A2A receptor antagonist and an antidepressant drug are effective for treating depression (Abstract). Greenlee et. al. also teaches that antidepressant drugs beneficial in combination with an adenosine A2A receptor antagonist include selective serotonin reuptake inhibitors, such as fluoxetine (p. 20, lines 21-23). While Greenlee et. al. does not explicitly teach that the hydrochloride salt of fluoxetine can be utilized, the hydrochloride salt of fluoxetine is well known in the art as the antidepressant 'Prozac'. Therefore, as the hydrochloride salt form of fluoxetine is also widely known as an antidepressant, it would have been obvious to utilize this particular salt form.

While Greenlee et. al. teaches that the combination of an adenosine receptor antagonist and a selective serotonin reuptake inhibitor such as fluoxetine or fluoxetine hydrochloride is advantageous for the treatment of depression, Greenlee et. al. does not explicitly teach that the adenosine A2A receptor antagonist is (E)-8-(3,4-dimethoxystyryl)-1,3-diethyl-7-methyl-3,7-dihydro-1H-purine-2,6-dione.

Shimada et. al. teaches that the compound, (E)-8-(3,4-dimethoxystyryl)-1,3-diethyl-7-methyl-3,7-dihydro-1H-purine-2,6-dione is beneficial for treating neurodegenerative disorders (column 9, claim 1). Shimada et. al. also teaches that (E)-8-(3,4-dimethoxystyryl)-1,3-diethyl-7-methyl-3,7-dihydro-1H-purine-2,6-

dione is an adenosine A2A receptor antagonist which is known as an antidepressant (column 1, lines 10-15).

One of ordinary skill in the art would have been motivated, at the time of the invention, to substitute the adenosine A2A receptor antagonist, (E)-8-(3,4-dimethoxystyryl)-1,3-diethyl-7-methyl-3,7-dihydro-1H-purine-2,6-dione, in the composition taught by Greenlee et. al., because Shimada et. al. teaches that (E)-8-(3,4-dimethoxystyryl)-1,3-diethyl-7-methyl-3,7-dihydro-1H-purine-2,6-dione is an adenosine A2A receptor antagonist with anti-depressive properties, and Greenlee et. al. teaches that the combination of an adenosine A2A receptor antagonist and a selective serotonin reuptake inhibitor such as fluoxetine hydrochloride is effective for treating depression. As it is taught by Shimada et. al. that (E)-8-(3,4-dimethoxystyryl)-1,3-diethyl-7-methyl-3,7-dihydro-1H-purine-2,6-dione is an adenosine A2A antagonist with anti-depressant activity, one of ordinary skill in the art would have expected success in substituting this agent in the composition taught by Greenlee et. al.

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory

action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SARAH PIHONAK whose telephone number is (571)270-7710. The examiner can normally be reached on Monday-Thursday 8:00 AM - 6:30 PM EST, with Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571)272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

S.P.

/SREENI PADMANABHAN/
Supervisory Patent Examiner, Art Unit 1627